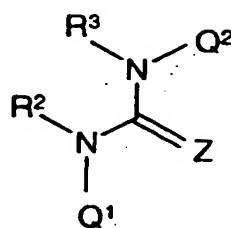


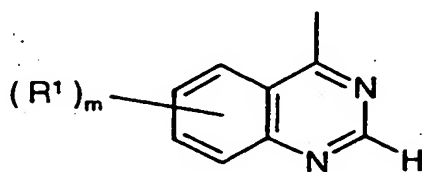
CLAIMS

- 5 1. A quinazoline derivative of the Formula I

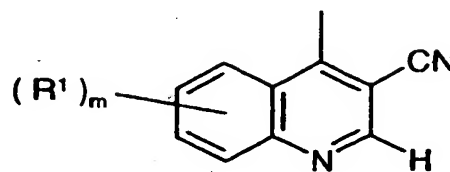


I

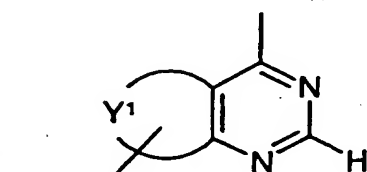
wherein Q<sup>1</sup> is a quinazoline-like ring such as a group of the formula Ia, Ib, Ic or Id



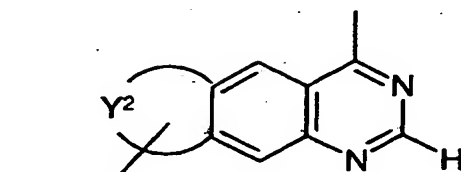
Ia



Ib



Ic



Id

- 10 wherein :

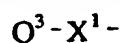
Y<sup>1</sup> together with the carbon atoms to which it is attached forms a 5- or 6-membered aromatic or partially unsaturated ring comprising 1 to 3 heteroatoms selected from O, N and S provided that the group of formula Ic so formed is not a purine ring;

- 15 Y<sup>2</sup> together with the carbon atoms to which it is attached forms a 5- or 6-membered aromatic or partially unsaturated ring comprising 1 to 3 heteroatoms selected from O, N and S;

m is 0, 1, 2, 3 or 4;

each R<sup>1</sup> group, which may be the same or different, is selected from halogeno, trifluoromethyl, cyano, isocyano, nitro, hydroxy, mercapto, amino, formyl, carboxy,

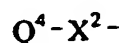
carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulphinyl, (1-6C)alkylsulphonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino, N-(1-6C)alkylsulphamoyl, N,N-di-[(1-6C)alkyl]sulphamoyl, (1-6C)alkanesulphonylamino and N-(1-6C)alkyl-(1-6C)alkanesulphonylamino, or from a group of the formula :



10 wherein  $X^1$  is a direct bond or is selected from O, S, SO, SO<sub>2</sub>, N(R<sup>4</sup>), CO, CH(OR<sup>4</sup>), CON(R<sup>4</sup>), N(R<sup>4</sup>)CO, SO<sub>2</sub>N(R<sup>4</sup>), N(R<sup>4</sup>)SO<sub>2</sub>, OC(R<sup>4</sup>)<sub>2</sub>, SC(R<sup>4</sup>)<sub>2</sub> and N(R<sup>4</sup>)C(R<sup>4</sup>)<sub>2</sub>, wherein R<sup>4</sup> is hydrogen or (1-6C)alkyl, and Q<sup>3</sup> is aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl, or (R<sup>1</sup>)<sub>m</sub> is (1-3C)alkylenedioxy,

15 and wherein adjacent carbon atoms in any (2-6C)alkylene chain within a R<sup>1</sup> substituent are optionally separated by the insertion into the chain of a group selected from O, S, SO, SO<sub>2</sub>, N(R<sup>5</sup>), CO, CH(OR<sup>5</sup>), CON(R<sup>5</sup>), N(R<sup>5</sup>)CO, SO<sub>2</sub>N(R<sup>5</sup>), N(R<sup>5</sup>)SO<sub>2</sub>, CH=CH and C≡C wherein R<sup>5</sup> is hydrogen or (1-6C)alkyl,

and wherein any CH<sub>2</sub>=CH- or HC≡C- group within a R<sup>1</sup> substituent optionally bears at  
20 the terminal CH<sub>2</sub>= or HC≡ position a substituent selected from halogeno, carboxy, carbamoyl, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl and di-[(1-6C)alkyl]amino-(1-6C)alkyl or from a group of the formula :



25 wherein  $X^2$  is a direct bond or is selected from CO and N(R<sup>6</sup>)CO, wherein R<sup>6</sup> is hydrogen or (1-6C)alkyl, and Q<sup>4</sup> is aryl, aryl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl,

and wherein any CH<sub>2</sub> or CH<sub>3</sub> group within a R<sup>1</sup> substituent optionally bears on each  
30 said CH<sub>2</sub> or CH<sub>3</sub> group one or more halogeno substituents or a substituent selected from hydroxy, cyano, amino, carboxy, carbamoyl, (1-6C)alkyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylsulphinyl, (1-6C)alkylsulphonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl,

- 150 -

(2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulphamoyl, N,N-di-[(1-6C)alkyl]sulphamoyl, (1-6C)alkanesulphonylamino and N-(1-6C)alkyl-(1-6C)alkanesulphonylamino, or from a group of the formula :

5  $-X^3-Q^5$

wherein  $X^3$  is a direct bond or is selected from O, S, SO, SO<sub>2</sub>, N(R<sup>7</sup>), CO, CH(OR<sup>7</sup>), CON(R<sup>7</sup>), N(R<sup>7</sup>)CO, SO<sub>2</sub>N(R<sup>7</sup>), N(R<sup>7</sup>)SO<sub>2</sub>, C(R<sup>7</sup>)<sub>2</sub>O, C(R<sup>7</sup>)<sub>2</sub>S and N(R<sup>7</sup>)C(R<sup>7</sup>)<sub>2</sub>, wherein R<sup>7</sup> is hydrogen or (1-6C)alkyl, and Q<sup>5</sup> is aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-  
10 (1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl,

and wherein any aryl, heteroaryl or heterocyclyl group within a substituent on R<sup>1</sup> optionally bears 1, 2 or 3 substituents, which may be the same or different, selected from halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy,  
15 (1-6C)alkylthio, (1-6C)alkylsulphinyl, (1-6C)alkylsulphonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulphamoyl, N,N-di-[(1-6C)alkyl]sulphamoyl, (1-6C)alkanesulphonylamino and N-(1-6C)alkyl-  
20 (1-6C)alkanesulphonylamino, or from a group of the formula :

$-X^4-R^8$

wherein  $X^4$  is a direct bond or is selected from O and N(R<sup>9</sup>), wherein R<sup>9</sup> is hydrogen or (1-6C)alkyl, and R<sup>8</sup> is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di-[(1-6C)alkyl]amino-  
25 (1-6C)alkyl, (2-6C)alkanoylamino-(1-6C)alkyl or (1-6C)alkoxycarbonylamino-(1-6C)alkyl, or from a group of the formula :

$-X^5-Q^6$

wherein  $X^5$  is a direct bond or is selected from O and N(R<sup>10</sup>), wherein R<sup>10</sup> is hydrogen or (1-6C)alkyl, and Q<sup>6</sup> is aryl, aryl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl  
30 or heterocyclyl-(1-6C)alkyl, and any Q<sup>6</sup> group optionally bears 1 or 2 substituents, which may be the same or different, selected from halogeno, (1-6C)alkyl and (1-6C)alkoxy,

and wherein any heterocyclyl group within a substituent on R<sup>1</sup> optionally bears 1 or 2 oxo or thioxo substituents;

202019945-1010702

$R^2$  is hydrogen or (1-6C)alkyl and  $R^3$  is hydrogen or (1-6C)alkyl, or  $R^2$  and  $R^3$  together form a  $CH_2$ ,  $(CH_2)_2$  or  $(CH_2)_3$  group;

$Z$  is O, S,  $N(C\equiv N)$  or  $N(R^{11})$ , wherein  $R^{11}$  is hydrogen or (1-6C)alkyl; and

$Q^2$  is aryl, aryl-(1-3C)alkyl, aryl-(3-7C)cycloalkyl, heteroaryl, heteroaryl-(1-3C)alkyl  
 5 or heteroaryl-(3-7C)cycloalkyl wherein each aryl group is phenyl or naphthyl and each heteroaryl group is a 5- or 6-membered monocyclic or a 9- or 10-membered bicyclic heteroaryl ring containing 1 or 2 nitrogen heteroatoms and optionally containing a further heteroatom selected from nitrogen, oxygen and sulphur, and  
 $Q^2$  is optionally substituted with 1, 2, 3 or 4 substituents, which may be the same or different,  
 10 selected from halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulphinyl, (1-6C)alkylsulphonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl,  
 15 (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino, N-(1-6C)alkylsulphamoyl, N,N-di-[(1-6C)alkyl]sulphamoyl, (1-6C)alkanesulphonylamino and N-(1-6C)alkyl-(1-6C)alkanesulphonylamino, or from a group of the formula :

20  $-X^6-R^{12}$

wherein  $X^6$  is a direct bond or is selected from O and  $N(R^{13})$ , wherein  $R^{13}$  is hydrogen or (1-6C)alkyl, and  $R^{12}$  is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl or di-[(1-6C)alkyl]amino-(1-6C)alkyl, or from a group of the formula :

25  $-X^7-Q^7$

wherein  $X^7$  is a direct bond or is selected from O, S, SO,  $SO_2$ ,  $N(R^{14})$ , CO,  $CH(OR^{14})$ ,  $CON(R^{14})$ ,  $N(R^{14})CO$ ,  $SO_2N(R^{14})$ ,  $N(R^{14})SO_2$ ,  $C(R^{14})_2O$ ,  $C(R^{14})_2S$  and  $C(R^{14})_2N(R^{14})$ , wherein each  $R^{14}$  is hydrogen or (1-6C)alkyl, and  $Q^7$  is aryl, aryl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl, or  $Q^2$  is optionally  
 30 substituted with a (1-3C)alkylenedioxy group,

and wherein any aryl, heteroaryl or heterocyclyl group within a substituent on  $Q^2$  optionally bears 1, 2 or 3 substituents, which may be the same or different, selected from

ART 34 AMDT

- halogeno, trifluoromethyl, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulphinyl, (1-6C)alkylsulphonyl, (1-6C)alkylamino, 5 di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulphamoyl, N,N-di-[(1-6C)alkyl]sulphamoyl, (1-6C)alkanesulphonylamino and N-(1-6C)alkyl-(1-6C)alkanesulphonylamino, or from a group of the formula :



wherein  $X^8$  is a direct bond or is selected from O and N( $R^{16}$ ), wherein  $R^{16}$  is hydrogen or (1-6C)alkyl, and  $R^{15}$  is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl or di-[(1-6C)alkyl]amino-(1-6C)alkyl,

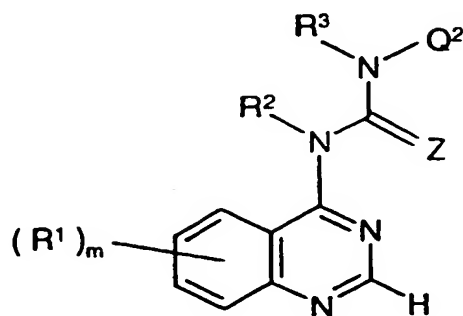
- 15 and wherein any heterocyclyl group within a substituent on  $Q^2$  optionally bears 1 or 2 oxo or thioxo substituents;

or a pharmaceutically-acceptable salt thereof;

provided that the compounds :-

- 1-(6,7-dimethoxyquinazolin-4-yl)-3-phenylurea,  
20 1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-phenylurea,  
1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-bromophenyl)urea,  
1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-methoxyphenyl)urea.  
1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
25 1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and  
30 1-{8-[3,4-dihydroxy-5(N-ethylcarbamoyl)tetrahydrofuran-2-yl]-7,8-dihydropteridin-4-yl}-3-(4-nitrophenyl)urea are excluded.

## 2. A quinazoline derivative of the Formula II



II

wherein each of  $m$ ,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $Z$  and  $Q^2$  has any of the meanings defined in claim 1;  
or a pharmaceutically-acceptable salt thereof;

## 5 provided that the compounds :-

1-(6,7-dimethoxyquinazolin-4-yl)-3-phenylurea,

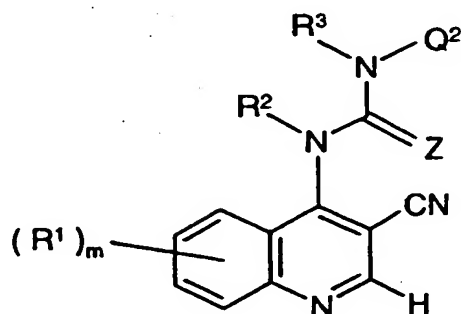
1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-phenylurea,

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-bromophenyl)urea and

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-methoxyphenyl)urea are excluded.

10

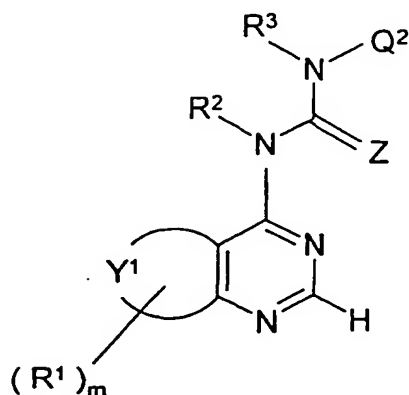
## 3. A quinoline derivative of the Formula III



III

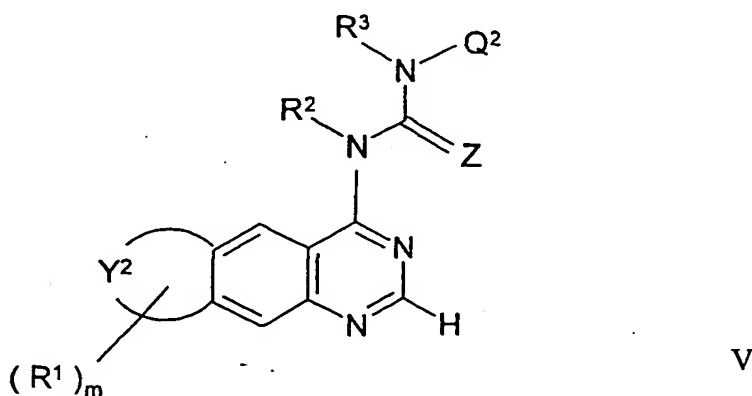
wherein each of  $m$ ,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $Z$  and  $Q^2$  has any of the meanings defined in claim 1;  
or a pharmaceutically-acceptable salt thereof.

4. A pyrimidine derivative of the Formula IV



- wherein each of  $m$ ,  $R^1$ ,  $Y^1$ ,  $R^2$ ,  $R^3$ ,  $Z$  and  $Q^2$  has any of the meanings defined in claim 1;  
 5 or a pharmaceutically-acceptable salt thereof;  
 provided that the compounds :-  
 1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 10 1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and  
 1-{8-[3,4-dihydroxy-5(*N*-ethylcarbamoyl)tetrahydrofuran-2-yl]-7,8-dihydropteridin-4-yl}-  
 15 3-(4-nitrophenyl)urea are excluded.

5. A quinazoline derivative of the Formula V



- wherein each of  $m$ ,  $R^1$ ,  $Y^2$ ,  $R^2$ ,  $R^3$ ,  $Z$  and  $Q^2$  has any of the meanings defined in claim 1;  
 20 or a pharmaceutically-acceptable salt thereof.

6. A quinazoline derivative of the Formula II according to claim 2 wherein :

m is 1 and the R<sup>1</sup> group is located at the 6- or 7-position and is selected from methoxy,

benzyloxy, cyclopropylmethoxy, 2-dimethylaminoethoxy, 2-diethylaminoethoxy,

3-dimethylaminopropoxy, 3-diethylaminopropoxy, 2-(1,2,3-triazol-1-yl)ethoxy,

5 3-(1,2,3-triazol-1-yl)propoxy, pyrid-2-ylmethoxy, pyrid-3-ylmethoxy, 2-pyrid-2-ylethoxy,

2-pyrid-3-ylethoxy, 2-pyrid-4-ylethoxy, 3-pyrid-2-ylpropoxy, 3-pyrid-3-ylpropoxy,

3-pyrid-4-ylpropoxy, 2-pyrrolidin-1-ylethoxy, 3-pyrrolidin-1-ylpropoxy, pyrrolidin-3-yloxy,

N-methylpyrrolidin-3-yloxy, pyrrolidin-2-ylmethoxy, N-methylpyrrolidin-2-ylmethoxy,

2-pyrrolidin-2-ylethoxy, 2-(N-methylpyrrolidin-2-yl)ethoxy, 3-pyrrolidin-2-ylpropoxy,

10 3-(N-methylpyrrolidin-2-yl)propoxy, 2-(2-oxoimidazolidin-1-yl)ethoxy, 2-morpholinoethoxy,

3-morpholinopropoxy, 2-(1,1-dioxotetrahydro-4H-1,4-thiazin-4-yl)ethoxy,

3-(1,1-dioxotetrahydro-4H-1,4-thiazin-4-yl)propoxy, 2-piperidinoethoxy,

3-piperidinopropoxy, piperidin-3-yloxy, piperidin-4-yloxy, N-methylpiperidin-4-yloxy,

piperidin-3-ylmethoxy, N-methylpiperidin-3-ylmethoxy, 2-piperidin-3-ylethoxy,

15 2-(N-methylpiperidin-3-yl)ethoxy, piperidin-4-ylmethoxy, N-methylpiperidin-4-ylmethoxy,

2-piperidin-4-ylethoxy, 2-(N-methylpiperidin-4-yl)ethoxy, 3-(4-aminomethylpiperidin-

1-yl)propoxy, 3-(4-tert-butoxycarbonylaminopiperidin-1-yl)propoxy,

3-(4-carbamoylpiperidin-1-yl)propoxy, 2-piperazin-1-ylethoxy, 3-piperazin-1-ylpropoxy,

2-(4-methylpiperazin-1-yl)ethoxy, 3-(4-methylpiperazin-1-yl)propoxy,

20 4-morpholinobut-2-en-1-yloxy, 4-morpholinobut-2-yn-1-yloxy,

2-(2-morpholinoethoxy)ethoxy, 2-methylsulphonylethoxy, 3-methylsulphonylpropoxy,

2-[N-(2-methoxyethyl)-N-methylamino]ethoxy, 3-[N-(2-methoxyethyl)-

N-methylamino]propoxy, 2-(2-methoxyethoxy)ethoxy, 3-methylamino-1-propynyl,

3-dimethylamino-1-propynyl, 3-diethylamino-1-propynyl, 6-methylamino-1-hexynyl,

25 6-dimethylamino-1-hexynyl, 3-(pyrrolidin-1-yl)-1-propynyl, 3-(piperidino)-1-propynyl,

3-(morpholino)-1-propynyl, 3-(4-methylpiperazin-1-yl)-1-propynyl,

6-(pyrrolidin-1-yl)-1-hexynyl, 6-(piperidino)-1-hexynyl, 6-(morpholino)-1-hexynyl,

6-(4-methylpiperazin-1-yl)-1-hexynyl, piperazin-1-yl, 4-methylpiperazin-1-yl,

3-imidazol-1-ylpropylamino, 3-pyrrolidin-1-ylpropylamino, 3-morpholinopropylamino,

30 3-piperidinopropylamino and 3-piperazin-1-ylpropylamino,

or m is 2 and the R<sup>1</sup> groups are located at the 6- and 7-positions, one R<sup>1</sup> group is located at the 6- or 7-position and is selected from the groups defined immediately hereinbefore and the other R<sup>1</sup> group is a methoxy group;



- 156 -

R<sup>2</sup> is hydrogen or methyl;

R<sup>3</sup> is hydrogen;

Z is O, S, NH or N(Et); and

Q<sup>2</sup> is phenyl, benzyl or phenethyl which optionally bears 1, 2 or 3 substituents, which  
5 may be the same or different, selected from fluoro, chloro, bromo, trifluoromethyl, nitro, methyl, ethyl and methoxy provided that at least one substituent is located at an ortho position;  
or a pharmaceutically-acceptable acid-addition salt thereof;  
and provided that 1-(6,7-dimethoxyquinazolin-4-yl)-3-phenylurea is excluded.

10

7. A quinazoline derivative of the Formula II according to claim 2 wherein :

m is 1 and the R<sup>1</sup> group is located at the 7-position and is selected from

3-(1,2,3-triazol-1-yl)propoxy, 2-pyrid-4-ylethoxy, 2-pyrrolidin-1-ylethoxy,

3-pyrrolidin-1-ylpropoxy, 2-morpholinoethoxy, 3-morpholinopropoxy,

15 2-(1,1-dioxotetrahydro-4H-1,4-thiazin-4-yl)ethoxy, 3-(1,1-dioxotetrahydro-4H-1,4-thiazin-

4-yl)propoxy, 2-piperidinoethoxy, 3-piperidinopropoxy, piperidin-3-ylmethoxy,

N-methylpiperidin-3-ylmethoxy, piperidin-4-ylmethoxy, N-methylpiperidin-4-ylmethoxy,

2-(4-methylpiperazin-1-yl)ethoxy, 3-(4-methylpiperazin-1-yl)propoxy,

4-pyrrolidin-1-ylbut-2-en-1-yloxy, 4-morpholinobut-2-en-1-yloxy,

20 4-morpholinobut-2-yn-1-yloxy, 3-methylsulphonylpropoxy and 2-[N-(2-methoxyethyl)-N-methylamino]ethoxy;

or m is 2 and one R<sup>1</sup> group is located at the 7-position and is selected from the groups defined immediately hereinbefore and the other R<sup>1</sup> group is a 6-methoxy group;

R<sup>2</sup> is hydrogen or methyl;

25 R<sup>3</sup> is hydrogen;

Z is O, S, NH or N(Et); and

Q<sup>2</sup> is phenyl which bears 1, 2 or 3 substituents, which may be the same or different, selected from fluoro, chloro, bromo, trifluoromethyl, nitro, methyl, ethyl and methoxy provided that at least one substituent is located at an ortho position;

30 or a pharmaceutically-acceptable acid-addition salt thereof.

20/2070-5465 FOOT

8. A quinazoline derivative of the Formula II according to claim 2 wherein :

m is 1 and the R<sup>1</sup> group is located at the 7-position and is selected from

3-(1,2,3-triazol-1-yl)propoxy, 2-pyrid-4-ylethoxy, 3-pyrrolidin-1-ylpropoxy,

3-morpholinopropoxy, 3-(1,1-dioxotetrahydro-4H-1,4-thiazin-4-yl)propoxy,

5 2-piperidinoethoxy, 3-piperidinopropoxy, N-methylpiperidin-4-ylmethoxy,

3-(4-methylpiperazin-1-yl)propoxy, 4-morpholinobut-2-en-1-yloxy, 4-morpholinobut-2-yn-

1-yloxy, 3-methylsulphonylpropoxy and 2-[N-(2-methoxyethyl)-N-methylamino]ethoxy;

or m is 2 and one R<sup>1</sup> group is located at the 7-position and is selected from the groups defined immediately hereinbefore and the other R<sup>1</sup> group is a 6-methoxy group;

10 R<sup>2</sup> is hydrogen or methyl;

R<sup>3</sup> is hydrogen;

Z is O; and

Q<sup>2</sup> is phenyl which bears 1, 2 or 3 substituents, which may be the same or different, selected from fluoro, chloro, bromo and trifluoromethyl provided that at least one substituent

15 is located at an ortho position;

or a pharmaceutically-acceptable acid-addition salt thereof.

9. A quinazoline derivative of the Formula II according to claim 2 selected from:-

1-(2,6-dichlorophenyl)-3-[7-(3-morpholinopropoxy)quinazolin-4-yl]urea,

20 1-(2,6-dichlorophenyl)-3-{7-[3-(1,1-dioxotetrahydro-4H-1,4-thiazin-4-yl)propoxy]quinazolin-4-yl}urea,

1-benzyl-3-[6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazolin-4-yl]urea,

1-phenethyl-3-[6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazolin-4-yl]urea,

1-(2,6-dichlorophenyl)-3-[6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazolin-4-yl]urea,

25 1-(2,6-difluorophenyl)-3-[6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazolin-4-yl]urea,

1-(2,6-dimethylphenyl)-3-[6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazolin-4-yl]urea,

1-(2-chloro-6-methylphenyl)-3-[6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazolin-

30 4-yl]urea,

1-(2,6-difluorophenyl)-3-[6-methoxy-7-(3-morpholinopropoxy)quinazolin-4-yl]urea,

1-(2,6-difluorophenyl)-3-[6-methoxy-7-[3-(4-methylpiperazin-1-yl)propoxy]quinazolin-4-yl]urea,

1-(2,6-dimethylphenyl)-3-[6-methoxy-7-[3-(4-methylpiperazin-1-yl)propoxy]quinazolin-4-yl]urea,

1-(2,6-dimethylphenyl)-3-[6-methoxy-7-(3-piperidinopropoxy)quinazolin-4-yl]urea,

1-(2,6-dimethylphenyl)-3-[6-methoxy-7-(N-methylpiperidin-4-ylmethoxy)quinazolin-

5 4-yl]thiourea and

1-(2-chloro-6-methylphenyl)-3-[6-methoxy-7-(3-pyrrolidin-1-ylpropoxy)quinazolin-4-yl]guanidine;

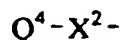
or a pharmaceutically-acceptable acid-addition salt thereof.

10. 10. A pyrimidine derivative of the Formula IV according to claim 4 wherein the fusion of ring Y<sup>1</sup> to the adjacent pyrimidine ring forms a thieno[3,2-*d*]pyrimidin-4-yl group;

m is 0, or m is 1 and the R<sup>1</sup> group is a methyl, ethyl, vinyl or ethynyl group which is located at the 6-position and bears a substituent selected from carboxy, carbamoyl,

N-(2-methylaminoethyl)carbamoyl, N-(2-dimethylaminoethyl)carbamoyl,

15 N-(3-methylaminopropyl)carbamoyl or N-(3-dimethylaminopropyl)carbamoyl, or from a group of the formula :



wherein X<sup>2</sup> is NHCO or N(Me)CO and Q<sup>4</sup> is 2-imidazol-1-ylethyl, 3-imidazol-1-ylpropyl, 2-pyridylmethyl, 4-pyridylmethyl, 2-pyrid-2-ylethyl, 2-pyrrolidin-1-ylethyl,

20 2-(2-oxopyrrolidin-1-yl)ethyl, 3-pyrrolidin-1-ylpropyl, 3-(2-oxopyrrolidin-1-yl)propyl, pyrrolidin-2-ylmethyl, 1-methylpyrrolidin-2-ylmethyl, 2-pyrrolidin-2-ylethyl,

2-(1-methylpyrrolidin-2-yl)ethyl, 3-pyrrolidin-2-ylpropyl, 3-(1-methylpyrrolidin-2-yl)propyl,

2-morpholinoethyl, 3-morpholinopropyl, 2-piperidinoethyl, 3-piperidinopropyl, piperidin-

3-ylmethyl, 1-methylpiperidin-3-ylmethyl, 2-piperidin-3-ylethyl, 2-(1-methylpiperidin-

25 3-yl)ethyl, piperidin-4-ylmethyl, 1-methylpiperidin-4-ylmethyl, 2-piperidin-4-ylethyl,

2-(1-methylpiperidin-4-yl)ethyl, 2-piperazin-1-ylethyl, 2-(4-methylpiperazin-1-yl)ethyl,

3-piperazin-1-ylpropyl or 3-(4-methylpiperazin-1-yl)propyl,

R<sup>2</sup> is hydrogen or methyl;

R<sup>3</sup> is hydrogen;

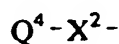
30 Z is O; and

Q<sup>2</sup> is phenyl, benzyl or phenethyl which optionally bears 1, 2 or 3 substituents, which may be the same or different, selected from fluoro, chloro, bromo, trifluoromethyl and methyl;

or a pharmaceutically-acceptable acid-addition salt thereof.

11. A pyrimidine derivative of the Formula IV according to claim 4 wherein the fusion of ring Y<sup>1</sup> to the adjacent pyrimidine ring forms a thieno[3,2-*d*]pyrimidin-4-yl group;

5 m is 0, or m is 1 and the R<sup>1</sup> group is a vinyl group located at the 6-position which bears at the terminal CH<sub>2</sub>= position a substituent selected from N-(2-dimethylaminoethyl)carbamoyl or N-(3-dimethylaminopropyl)carbamoyl, or from a group of the formula :



10 wherein X<sup>2</sup> is NHCO or N(Me)CO and Q<sup>4</sup> is 2-pyridylmethyl, 4-pyridylmethyl, 2-pyrid-2-ylethyl, 2-pyrrolidin-1-ylethyl, 3-(2-oxopyrrolidin-1-yl)propyl, 3-morpholinopropyl, 2-piperidinoethyl or 3-(4-methylpiperazin-1-yl)propyl,

R<sup>2</sup> is hydrogen or methyl;

R<sup>3</sup> is hydrogen;

15 Z is O; and

Q<sup>2</sup> is phenyl which bears 1, 2 or 3 substituents, which may be the same or different, selected from fluoro, chloro, bromo and trifluoromethyl provided that at least one substituent is located at the ortho position;

or a pharmaceutically-acceptable acid-addition salt thereof.

20

12. A pyrimidine derivative of the Formula IV according to claim 4 selected from:-

1-(2,6-dichlorophenyl)-3-(thieno[3,2-*d*]pyrimidin-4-yl)urea and

(*E*)-3-{4-[3-(2,6-dichlorophenyl)ureido]thieno[3,2-*d*]pyrimidin-6-yl}-

N-(3-dimethylaminopropyl)acrylamide;

25 or a pharmaceutically-acceptable acid-addition salt thereof.

13. A process for the preparation of a quinazoline derivative of the Formula I, or a pharmaceutically-acceptable salt thereof, according to claim 1 which comprises :-

(a) for those compounds of the Formula I wherein R<sup>3</sup> is hydrogen and Z is oxygen, the

30 reaction of an amine of the Formula VI



VI

10019945-010702

wherein  $Q^1$  and  $R^2$  have any of the meanings defined in claim 1 except that any functional group is protected if necessary, with an isocyanate of the Formula VII, or a conventional chemical equivalent thereof or a conventional chemical precursor thereof,



- 5 wherein  $Q^2$  has any of the meanings defined in claim 1 except that any functional group is protected if necessary, whereafter any protecting group that is present is removed by conventional means;

(b) for those compounds of the Formula I wherein  $R^3$  is hydrogen and Z is sulphur, the reaction of an amine of the Formula VI

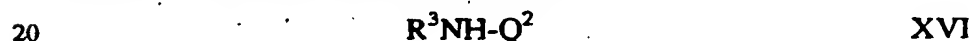


wherein  $Q^1$  and  $R^2$  have any of the meanings defined in claim 1 except that any functional group is protected if necessary, with an isothiocyanate of the Formula XII, or a conventional chemical equivalent thereof or a conventional chemical precursor thereof,



- 15 wherein  $Q^2$  has any of the meanings defined in claim 1 except that any functional group is protected if necessary, whereafter any protecting group that is present is removed by conventional means;

(c) for those compounds of the Formula I wherein  $R^2$  is hydrogen and Z is oxygen, the reaction of an amine of the Formula XVI



wherein  $Q^2$  and  $R^3$  have any of the meanings defined in claim 1 except that any functional group is protected if necessary, with an isocyanate of the Formula XVII, or a conventional chemical equivalent thereof or a conventional chemical precursor thereof,

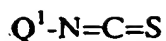


- 25 wherein  $Q^1$  has any of the meanings defined in claim 1 except that any functional group is protected if necessary, whereafter any protecting group that is present is removed by conventional means;

(d) for those compounds of the Formula I wherein  $R^2$  is hydrogen and Z is sulphur, the reaction of an amine of the Formula XVI



wherein  $Q^2$  and  $R^3$  have any of the meanings defined in claim 1 except that any functional group is protected if necessary, with an isothiocyanate of the Formula XXII, or a conventional chemical equivalent thereof or a conventional chemical precursor thereof,



XXII

wherein  $Q^1$  has any of the meanings defined in claim 1 except that any functional group is protected if necessary, whereafter any protecting group that is present is removed by conventional means;

5 (e) for those compounds of the Formula I wherein a substituent on  $Q^1$  or  $Q^2$  contains an alkylcarbamoyl group or a substituted alkylcarbamoyl group, the reaction of the corresponding compound of Formula I wherein a substituent on  $Q^1$  or  $Q^2$  is a carboxy group, or a reactive derivative thereof, with an amine or substituted amine as appropriate;

(f) for those compounds of the Formula I wherein a substituent on  $Q^1$  or  $Q^2$  contains an amino-(1-6C)alkyl group, the cleavage of the corresponding compound of Formula I wherein a substituent on  $Q^1$  or  $Q^2$  is a protected amino-(1-6C)alkyl group;

(g) for those compounds of the Formula I wherein Z is a  $N(R^{11})$  group wherein  $R^{11}$  is hydrogen or (1-6C)alkyl, the reaction of a thiourea of the Formula I wherein  $Q^1$ ,  $Q^2$ ,  $R^2$  and  $R^3$  have any of the meanings defined in claim 1 except that any functional group is protected if  
15 necessary and Z is sulphur, with an amine of formula  $R^{11}NH_2$ , whereafter any protecting group that is present is removed by conventional means; or

(h) for those compounds of the Formula I wherein a substituent on  $Q^1$  or  $Q^2$  contains an amino group, the reduction of a corresponding compound of Formula I wherein a substituent on  $Q^1$  or  $Q^2$  contains a nitro group;

20 and when a pharmaceutically-acceptable salt of a quinazoline derivative of the Formula I is required it may be obtained using a conventional procedure.

14. A pharmaceutical composition which comprises a quinazoline derivative of the Formula I, or a pharmaceutically-acceptable salt thereof, according to claim 1 in association  
25 with a pharmaceutically-acceptable diluent or carrier.

15. The use of a quinazoline derivative of the Formula I, or a pharmaceutically-acceptable salt thereof, according to claim 1 but without the proviso that the group of formula Ic so formed is not a purine ring and including the compounds :-

30 1-(6,7-dimethoxyquinazolin-4-yl)-3-phenylurea,

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-phenylurea,

1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-bromophenyl)urea,

202010-5466100

- 1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-methoxyphenyl)urea.  
 1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 5 1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and  
 10 1-{8-[3,4-dihydroxy-5(N-ethylcarbamoyl)tetrahydrofuran-2-yl]-7,8-dihydropteridin-4-yl}-  
 3-(4-nitrophenyl)urea,  
 in the manufacture of a medicament for use in the prevention or treatment of T cell mediated  
 diseases or medical conditions in a warm-blooded animal such as man.
- 15 16. A method for the prevention or treatment of T cell mediated diseases or medical  
 conditions in a warm-blooded animal in need of such treatment which comprises  
 administering to said animal an effective amount of a quinazoline derivative of the Formula I,  
 or a pharmaceutically-acceptable salt thereof, according to claim 1 but without the proviso  
 that the group of formula Ic so formed is not a purine ring and including the compounds :-
- 20 1-(6,7-dimethoxyquinazolin-4-yl)-3-phenylurea,  
 1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-phenylurea,  
 1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-bromophenyl)urea,  
 1-[5-(4-methoxyphenoxy)quinazolin-4-yl]-3-(3-methoxyphenyl)urea.  
 1-phenyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 25 1-(2-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(3-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(4-chlorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-(2-fluorophenyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 1-benzyl-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea,  
 30 1-(3-phenylpropyl)-3-(pyrazolo[3,4-*d*]pyrimidin-4-yl)urea and  
 1-{8-[3,4-dihydroxy-5(N-ethylcarbamoyl)tetrahydrofuran-2-yl]-7,8-dihydropteridin-4-yl}-  
 3-(4-nitrophenyl)urea.